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| TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371 | | ATTORNEY'S DOCKET NUMBER WPT0006 |
| | | U.S. APPLICATION NO (IF KNOWN) 10/009277 |
| INTERNATIONAL APPLICATION NO. PCT/GB00/02259 | INTERNATIONAL FILING DATE 9 June 2000 | PRIORITY DATE CLAIMED 9 June 1999 |
| TITLE OF INVENTION MIXING APPARATUS AND METHOD OF MIXING DURING CONDUCTING AN ASSAY | | |
| APPLICANT(S) FOR DO/EO/US David ANDREWES, et al. | | |
| <p>Applicant herewith submits to the U.S. Designated/Elected Office (DO/EO/US) the following items and other information:</p> <ol style="list-style-type: none"> 1. <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371. 2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. 3. <input type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1). 4. <input checked="" type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date. 5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2)). <ol style="list-style-type: none"> a. <input type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau) b. <input checked="" type="checkbox"/> has been transmitted by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). 6. <input type="checkbox"/> A translation of the International Application into English (35 U.S.C. 371(c)(2)). 7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)). <ol style="list-style-type: none"> a. <input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau). b. <input type="checkbox"/> have been transmitted by the International Bureau. c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. d. <input type="checkbox"/> have not been made and will not be made. 8. <input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). 9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)) (unsigned). 10. <input type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)). <p>Items 11 to 16 below concern document(s) or information included:</p> <ol style="list-style-type: none"> 11. <input checked="" type="checkbox"/> PCT Search Report and International Preliminary Examination Report. 12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet is included. 13. <input checked="" type="checkbox"/> A FIRST preliminary amendment. 14. <input type="checkbox"/> A substitute specification. 15. <input type="checkbox"/> A change of power or attorney and/or address letter. 16. <input checked="" type="checkbox"/> Other items or information <p>Certificate of Mailing by Express Mail and Return Card; IDS, Form 1449 and copies of references; Check for \$1,704.00.</p> | | |

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| APPLICATION NO. (If known) 10/009277 | APPLICATION NO. (If known) | ATTORNEY'S DOCKET NO. WPT0006 |
| 17. <input checked="" type="checkbox"/> The following fees are submitted (Applicant is small entity) | | CALCULATIONS |
| BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)) | | |
| Search Report has been prepared by the EPO or JPO \$ | | |
| International preliminary examination fee paid to USPTO (37 CFR 1.482)..... \$ | | |
| No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid (37 CFR 1.445(a)(2)) paid to USPTO..... \$ | | |
| Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO... \$1,040.00 | | |
| International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4)... \$ | | |
| ENTER APPROPRIATE FEE AMOUNT = | | \$1,040.00 |
| Surcharge of \$130.00 for furnishing the oath or declaration later than 20 <input type="checkbox"/> 30 <input checked="" type="checkbox"/> months from the earliest claimed priority date (37 CFR 1.492(e)). | | \$ 130.00 |
| CLAIMS | NUMBER FILED | RATE |
| Total Claims | 31 - 20 = | 11 x \$ 18.00 |
| Independent Claims | 7 - 3 = | 4 x \$ 84.00 |
| | | + \$280.00 |
| TOTAL OF ABOVE CALCULATIONS = | | \$1,704.00 |
| Reduction by ½ for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28) | | \$0.00 |
| SUBTOTAL = | | \$0 |
| Processing fee of \$130.00 for furnishing the English translation later than 20 <input type="checkbox"/> 30 <input type="checkbox"/> months from the earliest claimed priority date (37 CFR 1.492(f)). | | \$0 |
| TOTAL NATIONAL FEE = | | \$0 |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) \$40.00 per property + | | + \$0 |
| TOTAL NATIONAL FEE = | | \$1,704.00 |
| | | Amount to be: refunded |
| | | charged |
| a. <input checked="" type="checkbox"/> | A check in the amount of \$1,704.00 to cover the above fees is enclosed. | |
| b. <input type="checkbox"/> | Please charge my Deposit Account No. _____ in the amount of \$_____ to cover the above fees. | |
| c. <input checked="" type="checkbox"/> | The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-1123. | |
| NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b) must be filed and granted to restore the application to pending status. | | |
| SEND ALL CORRESPONDENCE TO: | | |
| Carol W. BURTON, Esq. Hogan & Hartson, L.L.P. One Tabor Center Suite 1500 1200 Seventeenth Street Denver, Colorado 80202 | |  SIGNATURE |
| | | Eugene J. Bernard NAME |
| | | Reg. No. 42,320 |

Attorney Docket No. WPT0006
Client Matter No. 80469.0006

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
UNDER THE PATENT COOPERATION TREATY

In re Application of:

David ANDREWES, et al.

Serial No. Unassigned

Filed: December 7, 2001

For: APPARATUS, INSTRUMENT AND
DEVICE FOR CONDUCTING AN ASSAY

Examiner: Unassigned

Art Unit: Unassigned

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
2900 Crystal Drive
Arlington, VA 22202-3513

Sir:

Please amend the copy of PCT Patent Publication No. WO 00/76642 A2, filed herewith, as follows:

IN THE CLAIMS

Please cancel claims 32–35 without prejudice to the subject matter contained therein.

Please amend the claims 1–31 according to the attached sheets.

REMARKS

The amendment cancels claims 32–35, making claims 1–31 pending in the application. The amendment removes the multiple dependent claim format and reference numbers in the claims, and is not made to overcome any prior art references. Support for the amendment can be found in the claims. No new matter has been added by the amendment.

Please consider the pending claims in light of the references cited in the enclosed Information Disclosure Statement. These references were cited in the PCT International Search Report, a copy of which is enclosed for your convenience.

Applicants enclose herewith the fee for filing a continuation application and believe this to be the only fee required for this amendment and response. Should any additional fees be required, please charge Deposit Account 50-1123.

Respectfully submitted,

December 7, 2001



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MARKED-UP VERSION OF THE CLAIMS

1. A method of mixing a sample in a chamber [(3, 5)] comprising the steps of positioning a paddle [(100)] in the sample and causing said paddle to undergo a reciprocating motion.
2. A method as claimed in claim 1 wherein the paddle is of a magnetic material and comprises a liquid moving surface and means for supporting the paddle in or over the chamber and said paddle is caused to undergo a reciprocating motion by the action of an electromagnetic means.
3. A method as claimed in claim 2 wherein the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface which arms sit in a pair of slots in sides extending from a base which defines the chamber.
4. A method as claimed in [either] claim 2 [or 3] which [further] comprises the steps of detecting an analyte in said sample by passing a light beam from a light emitter through said chamber and an opening [(106)] formed in the liquid moving surface of said paddle to a light detector.
5. A method as claimed in claim 4 wherein the sample is glycated haemoglobin and is detected by a spectrophotometric means at between 405 nm and 460 nm.
6. A paddle [(100)] comprising a liquid moving surface and means for supporting said paddle in or over a chamber such that the paddle can undergo a reciprocating motion in the chamber.
7. A paddle as claimed in claim 6 wherein the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface.
8. A paddle as claimed in [either] claim 6 [or 7] wherein the paddle is T shaped.

9. A paddle as claimed in [any of] claim 6[,7 or 8] wherein the liquid moving surface has an opening [(106)] formed therein through which a light beam can pass.

10. A paddle as claimed in [any of] claim[s] 6 [to 9] wherein the paddle comprises a magnetic material.

11. A paddle as claimed in [any of] claim[s] 6 [to 9] wherein the paddle comprises a piezoelectric material.

12. A sample container comprising a chamber [(3, 5)] adapted to receive a paddle [(100)], said paddle being mounted in or over said chamber such that the paddle can undergo a reciprocating motion in the chamber.

13. A sample container as claimed in claim 12 comprising a base with sides extending therefrom to define the chamber, said sides comprising means which support the paddle.

14. A sample container as claimed in claim 13 wherein said means which support the paddle is a pair of slots in said sides.

15. A sample container as claimed in [any of] claim[s] 12[-14] in which said chamber is an optical chamber.

16. A sample container as claimed in [any of] claim[s] 12[-15] which is a carousel or cassette.

17. A [carousel] sample container as claimed in claim 16, which is a carousel for use in an assay in which a sample is separated into a first component fraction and a second component fraction, which fractions are presented to an instrument, comprising a first inlet which is or leads to a first component fraction collection chamber, a second inlet which is or leads to a second component fraction collection chamber, and an inlet port accommodating a filter means or a binder retaining means, said inlet port being movable relative to each of said first and second inlets such that the inlet port can be brought into liquid communication with each first and second inlet in turn as required.

18. A sample container as claimed in claim 16 which is a carousel comprising a base portion having a plurality of chambers including first and second inlets, a top portion which together with the base portion forms the carousel, and a funnel portion including an inlet port, said carousel being rotatably mounted about said funnel portion.

19. An [instrument] apparatus adapted to receive a sample container comprising a chamber adapted to receive a paddle, said instrument comprising means for causing said paddle to undergo a reciprocating motion in the chamber.

20. An apparatus as claimed in claim 19 in which said means for causing said paddle to undergo a reciprocating motion is an electromagnetic means.

21. An apparatus as claimed in claim 20 wherein said electromagnetic means is a solenoid.

22. A device comprising an instrument capable of detecting an analyte in a sample which is presented thereto in a sample container comprising a chamber adapted to receive a paddle said paddle being mounted in or over said chamber such that said paddle can undergo a reciprocating motion when initiated by said instrument.

23. A device, comprising an instrument for reading one or more samples, and an apparatus for presenting the one or more samples to the instrument, wherein the positioning of the one or more samples into a reading position is achieved using two phased recognition.

24. A device as claimed in claim 23 in which a first switch informs the instrument that the apparatus is within range and a second switches confirms precise alignment.

25. A device as claimed in claim 23 [or 24] wherein a first micro switch on the instrument is activated by an ["element"] on the apparatus and this constitutes the first phase of detection and a second switch on the

instrument serves as [the] a ["fine tune["] and is activated when the instrument reaches a precise location on the instrument.

26. A device as claimed in claim 25 wherein the ["element"] on the apparatus is a projecting member which depresses a board mounted micro-switch via a rocker arm assembly.

27. A device as claimed in claim 26 wherein the two members of the switch are a notch in the outermost wall of the apparatus, and a resilient member or arm on the instrument.

28. A device as claimed in claim 27 wherein the apparatus is a carousel or cassette type apparatus.

29. A device as claimed in claim 28 comprising four switches located 90° apart.

30. A method for determining the percentage glycation of blood comprising the steps of separating a blood sample into a first component fraction containing one or more non glycated proteins, and a second component containing the one or more glycated protein and detecting/quantifying glycated haemoglobin by spectrophotometric means at between 405 nm and 460 nm.

31. A method as claimed in claim 30 wherein the detection/quantification of glycated haemoglobin is measured at about 440 nm.

CLEAN VERSION OF THE CLAIMS

1. A method of mixing a sample in a chamber comprising the steps of positioning a paddle in the sample and causing said paddle to undergo a reciprocating motion.
2. A method as claimed in claim 1 wherein the paddle is of a magnetic material and comprises a liquid moving surface and means for supporting the paddle in or over the chamber and said paddle is caused to undergo a reciprocating motion by the action of an electromagnetic means.
3. A method as claimed in claim 2 wherein the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface which arms sit in a pair of slots in sides extending from a base which defines the chamber.
4. A method as claimed in claim 2 which comprises the steps of detecting an analyte in said sample by passing a light beam from a light emitter through said chamber and an opening formed in the liquid moving surface of said paddle to a light detector.
5. A method as claimed in claim 4 wherein the sample is glycated haemoglobin and is detected by a spectrophotometric means at between 405 nm and 460 nm.
6. A paddle comprising a liquid moving surface and means for supporting said paddle in or over a chamber such that the paddle can undergo a reciprocating motion in the chamber.
7. A paddle as claimed in claim 6 wherein the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface.
8. A paddle as claimed in claim 6 wherein the paddle is T shaped.
9. A paddle as claimed in claim 6 wherein the liquid moving surface has an opening formed therein through which a light beam can pass.

10. A paddle as claimed in claim 6 wherein the paddle comprises a magnetic material.

11. A paddle as claimed in claim 6 wherein the paddle comprises a piezoelectric material.

12. A sample container comprising a chamber adapted to receive a paddle, said paddle being mounted in or over said chamber such that the paddle can undergo a reciprocating motion in the chamber.

13. A sample container as claimed in claim 12 comprising a base with sides extending therefrom to define the chamber, said sides comprising means which support the paddle.

14. A sample container as claimed in claim 13 wherein said means which support the paddle is a pair of slots in said sides.

15. A sample container as claimed in claim 12 in which said chamber is an optical chamber.

16. A sample container as claimed in claim 12 which is a carousel or cassette.

17. A sample container as claimed in claim 16, which is a carousel for use in an assay in which a sample is separated into a first component fraction and a second component fraction, which fractions are presented to an instrument, comprising a first inlet which is or leads to a first component fraction collection chamber, a second inlet which is or leads to a second component fraction collection chamber, and an inlet port accommodating a filter means or a binder retaining means, said inlet port being movable relative to each of said first and second inlets such that the inlet port can be brought into liquid communication with each first and second inlet in turn as required.

18. A sample container as claimed in claim 16 which is a carousel comprising a base portion having a plurality of chambers including first and second inlets, a top portion which together with the base portion forms the carousel, and a funnel portion including an inlet port, said carousel being rotatably mounted about said funnel portion.

19. An apparatus adapted to receive a sample container comprising a chamber adapted to receive a paddle, said instrument comprising means for causing said paddle to undergo a reciprocating motion in the chamber,

20. An apparatus as claimed in claim 19 in which said means for causing said paddle to undergo a reciprocating motion is an electromagnetic means.

21. An apparatus as claimed in claim 20 wherein said electromagnetic means is a solenoid.

22. A device comprising an instrument capable of detecting an analyte in a sample which is presented thereto in a sample container comprising a chamber adapted to receive a paddle said paddle being mounted in or over said chamber such that said paddle can undergo a reciprocating motion when initiated by said instrument.

23. A device, comprising an instrument for reading one or more samples, and an apparatus for presenting the one or more samples to the instrument, wherein the positioning of the one or more samples into a reading position is achieved using two phased recognition.

24. A device as claimed in claim 23 in which a first switch informs the instrument that the apparatus is within range and a second switch confirms precise alignment.

25. A device as claimed in claim 23 wherein a first micro switch on the instrument is activated by an element on the apparatus and this constitutes the first phase of detection and a second switch on the instrument serves as a fine tune and is activated when the instrument reaches a precise location on the instrument.

26. A device as claimed in claim 25 wherein the element on the apparatus is a projecting member which depresses a board mounted micro-switch via a rocker arm assembly.

27. A device as claimed in claim 26 wherein the two members of the switch are a notch in the outermost wall of the apparatus, and a resilient member or arm on the instrument.

28. A device as claimed in claim 27 wherein the apparatus is a carousel or cassette type apparatus.

29. A device as claimed in claim 28 comprising four switches located 900 apart.

30. A method for determining the percentage glycation of blood comprising the steps of separating a blood sample into a first component fraction containing one or more non glycated proteins, and a second component containing the one or more glycated protein and detecting/quantifying glycated haemoglobin by spectrophotometric means at between 405 nm and 460 nm.

31. A method as claimed in claim 30 wherein the detection/quantification of glycated haemoglobin is measured at about 440 nm.

4/P&D

JC13 Rec'd PCT/PTO 07 DEC 2001

DESCRIPTIONMIXING APPARATUS AND METHOD OF MIXING

The present invention relates to an improved mixing apparatus and a method of mixing.

More particularly it relates to an improved apparatus, instrument and device for conducting an assay and the assay methodology.

In a particularly preferred embodiment it relates to a device suitable for use in assaying analyses, for example glaciated proteins, in samples such as, for example, blood.

A person skilled in the art will however appreciate that the principle behind the invention can be applied to solve a mixing problem in a number of different apparatus, instruments or devices.

The applicant has developed an apparatus, instrument and device for conducting an assay as disclosed in PCT/GB98/03586. The apparatus comprises a first inlet, a second inlet, and an inlet port, the inlet port being moveable relative to each of said first and second inlets such that the port can be brought into liquid communication with each inlet in turn as required, the inlet port accommodating a filter means and/or a binder retaining means.

In the course of conducting an assay to, for example, determine the presence or absence of one or more analyses in a sample, the sample is separated into a first component fraction and a second component fraction,

the second component fraction being obtained by eluting a component "held" on the binder retaining means from the binder retaining means.

The applicant has determined that the elution step in which the elutant fills the second inlet under gravity, gives a non-homogenous sample (due to the formation of an elution gradient in the second inlet) which results in inaccurate readings when the sample is "read" in a measuring instrument, such as, for example, an instrument comprising a microprocessor operable via a keypad, one or more light emitters and one or more light detectors, a display and driver, an analogue to digital convertor and means for connecting the instrument to a power source.

It is an aim of the present invention to provide a simple method for making a gravity fed fraction homogenous and more particularly to provide a modified apparatus, instrument and/or device capable of performing such a method.

In accordance with a first aspect of the present invention there is provided a method of mixing a sample in a chamber comprising positioning a paddle in the sample and causing said paddle to undergo a reciprocating motion.

It is another and independent aim of the present invention to provide an apparatus, instrument or device, capable of mixing a sample for an assay in which an analyte is detected by a spectrophotometric means and/or a component for use in achieving this aim.

According to a further aspect of the present invention there is provided, a paddle comprising a liquid moving surface and means for supporting said paddle in or over a chamber such that the paddle can undergo a reciprocating motion in the chamber.

Preferably the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface.

Preferably the paddle is T shaped.

More preferably the fluid moving surface has an opening formed therein through which a light beam can pass.

In one embodiment, the paddle comprises a magnetic material and is caused to undergo a reciprocating motion by an electromagnetic means such as a solenoid.

Of course other mechanisms could be used to effect a reciprocating motion. For example, the paddle could comprise a piezoelectric material and be caused to undergo a reciprocating motion using a localised current.

According to yet a further aspect of the present invention there is provided a sample container adapted to receive a paddle said paddle being mounted in or over said sample container such that the paddle can undergo a reciprocating motion in the container.

Preferably the sample container comprises a base with sides extending therefrom to define a chamber, said sides comprising means, for example a pair of slots, which support the paddle.

Preferably the sample container is an apparatus comprising an optical chamber.

More preferably the sample container is part of a carousel or cassette.

According to yet a still further aspect of the present invention there is provided an instrument adapted to receive a sample container comprising a paddle, said instrument comprising means for causing said paddle to undergo a reciprocating motion in the container.

Preferably said means for causing said paddle to undergo a reciprocating motion is an electromagnetic means, for example a solenoid.

According to yet a still further aspect of the present invention there is provided a device comprising a reading instrument comprising means for driving a paddle in a reciprocating manner in an apparatus comprising an optical chamber.

An example of an apparatus and instrument which can be adapted in accordance with the present invention are described in International application PCT/GB98/03586.

The apparatus and instrument described in PCT/GB98/03586 are susceptible to a number of other problems common to devices which are used in assays. Thus, a separate and unrelated problem with a device of the general type described in PCT/GB98/03586, namely one in which a sample or samples are presented to an instrument for reading, is one of accurately positioning the sample relative to, for example, one or more of the light

emitters and one or more light detectors which make up the reading means if reading errors are to be avoided or at least minimized.

Thus it is an independent aim of the present invention to provide a device which enables accurate readings to be taken.

According to this independent aspect of the present invention there is provided a device, comprising an instrument for reading one or more samples, and an apparatus for presenting the one or more samples to the instrument, wherein the positioning of the one or more samples into a reading position is achieved using two phased recognition.

The two phased recognition preferably utilises at least two independent micro switches.

A first switch informs the instrument that the apparatus is within range and a second switch confirms precise alignment.

A first micro switch on the instrument is activated by an "element" on the apparatus and this constitutes the first phase of detection. Preferably the element on the apparatus is a projecting member which depresses a board mounted micro-switch via a rocker arm assembly. The rocker arm actuation overcomes any error in the horizontal location of the switch on the circuit board.

A second switch on the instrument serves as the "fine tune" and is activated when the instrument reaches a precise (as opposed to general) location on the instrument.

In one embodiment the two members of the switch are a notch in the outermost wall of the apparatus, more particularly a carousel or cassette type apparatus, and a resilient member or arm on the instrument. When the carousel or cassette type apparatus moves into position the resilient member or arm moves from a position in which the member is biased to its unbiased position thereby deactivating the switch.

This two stage recognition makes assembly easier and increases the robustness of operation. It also improves the ease of use.

In the case of a carousel device of the type disclosed in PCT/GB98/03586, it is preferred that there are a plurality of such switches. More preferably there are four such switches located 90° apart.

A separate and unrelated problem with a device of the general type described in PCT/GB98/03586 is how to achieve good readings when quantifying two different fractions.

For example in the case of diabetes management it is desirable to determine the percentage of blood haemoglobin (Hb) that is glaciated. This means two assay results need to be obtained and a comparison made between them. For example between glaciated and non glaciated haemoglobin.

Traditionally analyses are measured at a peak frequency. In the case of glaciated proteins containing haem pigment this peak frequency is around 405nm. The applicant has determined that there are significant advantages

to be gained by making the measurements off peak, and in the case of glaciated haemoglobin protein, at between 415-460nm, more particularly still at about 440nm. This frequency range corresponds to be shoulder of the absorbance verses wavelength graph for haemoglobin. The 440 nm figure is the preferred wavelength. This extends the linear response to cover a wider and hence more useful range of haemoglobin concentrations.

According to this independent aspect of the present invention there is provided a method for determining the % glycation of blood comprising separating a blood sample into a first component fraction containing one or more non glaciated proteins, and a second component containing the one or more glaciated proteins, and detecting/quantifying the analyte by spectrophotometric means at between 405 nm and 460 nm, more preferably at about 440nm.

The "off peak" measurement avoids complicated calibration procedures, both in production and on-going in the field. It is essential for the performance of an instrument and when comparing tests between instruments that there is a linear response between measurement and concentration of absorbing substance. It is equally important that the range of linear response is wide enough so that measurement of, for example, both glaciated and unglycated fractions can be made on a linear portion of a response curve. The reason for this is that the slope of the linear response will vary for a number of reasons from instrument to instrument. Also the

slope of the linear response will also vary within an instrument as a function of temperature or other environmental factors. However, the nature of the calculation of % glycation is such that, within a given instrument, the slope of the response cancels out. Variations in slope do not therefore effect the result either within an instrument or between instruments, as long as significant change does not occur over the period of an assay. Any remaining variation between instruments can therefore be equalised using a calibrated offset established during initial set up at manufacture.

The use of a narrow band of wavelength produces a linear response but as this nears the absorbance maximum of haemoglobin the range of response is reduced. This is because at this point the system is at its maximum sensitivity. The selection of suitable band pass filters away from the absorbance maximum de-sensitises the system and extends the working range of the response allowing the elimination of slope factors described above. The reduced sensitivity is then offset by achieving a high signal to noise ratio on the detector electronics.

A separate and unrelated problem with a device of the general type described in PCT/GB98/03586 is ensuring accuracy of readings and keeping critical values (CV^s) to a minimum.

The applicant has demonstrated that a major factor effecting critical values is ensuring all of the sample is collected for measuring. Thus where small volumes are measured as much as 8% of the total volume can be lost

in a single drop.

According to this independent aspect of the present invention there is provided an apparatus incorporating one or a plurality of means for breaking the surface tension of a drop to ensure it leaves a first component part and enters a second component part of an apparatus.

In one embodiment the means comprise a web or like member situated between the first and second components parts.

More preferably the apparatus is of a type in which an inlet port is movable relative to each of first and second inlets, said inlet port being funnel shaped and accommodating a filter means or binder retaining means, said web being situated across the outlet of said funnel.

A separate and unrelated problem with a device of the general type described in PCT/GB98/03586 is the problem of ensuring the apparatus is firmly held in position in the apparatus when readings are to be taken.

The Applicant has resolved this problem by careful design of the apparatus and instrument.

Thus in one embodiment the carousel apparatus comprises a tapered circumferential ring and the instrument comprises spring clips which pull the carousel downwards preventing wobble.

According to this independent aspect of the present invention there is provided a device comprising an instrument for reading one or more samples and an apparatus for presenting the one or more sample to the instrument,

wherein the apparatus is held firmly in position in the instrument by means of spring clips.

The main invention and various independent aspects of the invention will now be described, by way of example only with reference to a device of the general type described in PCT/GB98/03586 and a method of assaying glaciated and non glaciated haemoglobin fractions.

FIG. 1 is a perspective view of an apparatus according to one aspect of the invention:

FIG. 2 is a partial sectional view of the Fig. 1 apparatus;

FIG. 3 is a perspective view of the base portion of the apparatus of FIG. 2 showing the paddle of the invention; and

FIG. 4 is a perspective view of an instrument for use with an apparatus as illustrated in FIGS 1 to 3.

Referring to Figs. 1 and 2 the carousel apparatus 31 comprises a base section 2 of clear plastics (shown in detail in Fig. 3), a top portion 6 and a funnel portion 32. The funnel portion 32 is made of a hydrophobic plastics and has a relatively large aperture to simplify emptying of reagents therein. It has an outlet 34 which directs the liquid into the optical chambers 3 and 5 when the apparatus is rotated in an instrument. The outlet 34 includes a frit (not shown) which frit serves to retain particles such as, for example, an amino phenyl boronate agarose affinity matrix. The funnel 32 which serves as an inlet port has an annular rim 36 with a recessed portion 38. The rim

36 partially overlies apertures 40, 42 and 44 formed in the top portion 6 of the apparatus such that tubes vertically disposed in the apparatus cannot pass through the respective apertures until the apertures are aligned with the recessed portion 38 of the annular rim. Projecting from the underside of the funnel is a stem 48 with a female mating member via which the apparatus 31 is connected to the instrument 24 which has a male member 50 adapted to engage it. The male member 50 holds the funnel in a fixed position relative to the instrument 24 such that the base portion 2 and top portion 6 of the apparatus 31 which together form a carousel rotate around the funnel, the annular rim 36 of the funnel serving as a guide means.

The base portion 6 of the apparatus is made of a clear plastics, is generally annular in shape and is divided into a plurality of compartments. As can be seen from Fig. 3 there are two optical chambers 3 and 5, a third chamber 4, for receiving waste from a wash step, which third chamber is disposed between optical chambers 3 and 5, and three additional chambers 40', 42' and 44' each housing a reagent tube. These chambers 40', 42' and 44', which are disposed below apertures 40, 42 and 44 in the top portion 6 of the apparatus 31, are arranged so that the reagent tubes are presented to the user when the carousel is in the appropriate position in use. The optical chambers have a curved outer wall 52 and a curved inner wall 54 of optical quality, which help focus light from the LED's of the instrument 24 through the sample in the chamber to photodiodes at the other side thereof.

Each optical chamber 3, 5 can be brought into liquid communication with the outlet 34 of the funnel inlet port 9. Alternatively, the optical chambers can be recessed. Extending outwardly from the outermost wall 56 of the base portion 2 is a guide member 58 which sits within a circumferential channel member 60 formed on the outermost wall 62 of the annular recess 64 of the instrument 24. A communicating channel 66 which extends from the channel member 60 in outermost wall 62 to the top face 68 of the instrument 24 allows the guide member 58 to be inserted into the channel member 60 when the apparatus 31 is connected to the instrument 24.

A projecting member or tab 70 on the knurled edge 72 of the top portion 6 acts as an indicator means, denoting the position for locating the apparatus on the instrument and serves to assist in the turning of the apparatus.

The base portion 2 is connected to the top portion and the funnel portion sits in a channel 76 formed by a step on the top surface 78 of the top portion 6.

The instrument illustrated in Fig. 4 has been designed for use with a basic apparatus as herein before described. The instrument is provided with a power management and monitoring circuit so that the instrument can be connected to, for example, an external dc supply or a car battery. Additionally, the instrument is provided with a communication system such as, for example, a RS232 thereby providing means for sending and receiving

instructions and down loading data.

Significantly, the means for receiving the apparatus is an annular recess 64 in the instrument which is defined by a floor, an outermost sidewall 62 and an innermost sidewall 80.

The floor of the annular recess comprises a ramp 82 on a part thereof. Within the outermost sidewall 62 of the annular recess is a channel member 60 and extending therefrom to the top surface a connecting channel 66.

In use the basic apparatus is inserted into the annular recess 60 by aligning guide member 58 of the apparatus with connecting channel 66 so that the apparatus is connected to male mating member 50 via its female mating member 48. The guide member 58 can thus enter channel member 60 such that it can be rotated. On rotation a first tube is directed up the ramp 82 and out of its aperture 44 since the recessed portion 38 of the annular ring 36 is aligned with the aperture. In this position the outlet 34 is in liquid communication with the first optical chamber 3 and the first step of the assay can be conducted. By turning the apparatus through a further 90° a wash solution is presented through aperture 42 for use and then on turning the apparatus though a further 90° tube 40, the eluting solution, is presented. In this manner the appropriate reagents are presented for each step of the assay process.

Having briefly described the favoured basic apparatus and instrument there follows a more detailed look at the improvements.

When tested an apparatus as described in PCT/GB98/03586 showed a critical value in the order of 6-7%. This was found to result primarily from an elution gradient forming when the glaciated fraction was eluted off the solid phase. In fact, it was found that the glaciated fraction was eluted off in a decreasing concentration as the elution buffer percolated into the optical chamber 5. Tests indicated that the first concentrated drops emerging from the funnel 32 collected in the corners of the optical chamber 5 and did not mix sufficiently with the more dilute drips that followed. As a result measurements taken before mechanical mixing of the solution showed poorer precision and an "off set" from those recorded post mixing.

To overcome this problem it proved necessary to introduce a mixing step.

However traditional methods proved unsuitable. Thus, for example, the apparatus could not be shaken without fear of damage to the instrument, and the use of a rotating flea or oscillating ball bearing could damage the optical chamber.

The applicant solved the problem using a paddle 100. A number of approaches were used:

Retention of a stirring device was seen as the major issue to be resolved. Attaching a stirring component to the side walls of the optical chamber was seen as a possible approach to overcome this problem. Two alternatives were investigated: In one embodiment the paddle was

clipped over the side walls of the optical chamber and the paddle was made to vibrate in the direction of the optical axis using an electromagnet. A hole in the centre of the paddle provides a path for the light from the LED.

In another embodiment the paddle was clipped over one side of the optical chamber 5 and was made to vibrate at right angles to the optical axis away from the light path.

Both these embodiments provided adequate mixing once a resonant frequency was found by adjusting the frequency of an oscillator driving an electromagnet. Though attractive there were still a number of problems with this approach.

As the paddle must retain stiffness a significant amount of energy was required to generate the oscillation. This would have implications for any battery operated instrument.

Furthermore resonant frequencies vary from component to component and with the liquid level within a chamber. Some means of scanning the frequencies would thus be required to hit resonance and thus ensure adequate mixing. Since both components also had a 3-dimensional shape forming was required increasing costs.

An alternative approach of using a flat paddle overcame the problems associated with the oscillating approach described above.

Thus in a preferred embodiment and as illustrated in Fig.3 a metal paddle 100 was retained in grooves 101 formed by building-up the side walls

102, 104 of the optical chamber 5. The paddle was able to reciprocate with minimal friction and could be forced to swing through the solution, along the direction of the optical axis, using an electromagnet positioned below the photodiode on the outer circumference of the platten moulding (described hereafter). A hole 106 is provided to enable the light from the LED to reach the detector.

As very little force is necessary to move the paddle, significantly less energy is required to drive the electromagnet. Experiments have shown that fewer than 10 swings of the paddle are required to produce a visually homogenous solution from a layered dye-water starting solution.

Effective retention of the paddle has been demonstrated by positioning a web (not shown) on the underside of the top moulding 6, just above the centre of the paddle.

Another improvement relates to the use of 2 micro-switches in a phased approach. This allows the precise unambiguous detection of the apparatus 31 in the instrument 24. One switch (not shown) at each of four locations is activated by a feature 58 (in this case also the guide member) on the circumference of the plastic well as it rotates. This depresses a board mounted micro-switch (not shown) via a rocker arm assembly (110, 112, 114 & 116) at each of the four operating positions (Fig. 4). The rocker arm actuation overcomes any error in the horizontal location of the switch on the circuit board (not shown). This constitutes the first phase of detection.

The second phase of detection is provided by a micro-switch which is activated by the operation of a ratchet arm not shown with a respective notch or notches 120, 122, (only two of the four are visible) in the outermost wall 56 of the carousel. A flange 131 extending from the ratchet arm contacts a switch on the instrument. The ratchet arm is biased such that when the carousel is in one of the four operating positions it moves into a notch in the carousel, deactivating the switch but when it is not in one of these positions it is acted against by the outermost wall 56 of the carousel causing the switch to be activated. These notches are preferably shaped to allow rotation in one direction only. These switches are only de-activated when the instrument and apparatus are in an exact location. The two phased approach makes assembly easier, increases robustness of operation and improves ease of use.

Finally another improvement relates to the arrangement used to overcome a 'wobble' problem. Any movement, however small, between the carousel and instrument can alter the path of light during reading. By modifying the carousel and instrument to provide a lock facility the reading problem was overcome.

In one embodiment the carousel comprises (Fig.1) a circumferential ring 124 comprising an inclined surface 126 and a flat surface 128.

The instrument 24 which receives the carousel comprises a casing 130, a printed circuit board 132 onto which is mounted a plateen 134 and a

hold down 136 comprising four spring clips 138, 140, 142, 144. When the carousel is inserted into the instrument, the spring clips ride up the inclined surface 126 and their claws lock against the flat surface 128.

CLAIMS

1. A method of mixing a sample in a chamber (3, 5) comprising positioning a paddle (100) in the sample and causing said paddle to undergo a reciprocating motion.

2. A method a claimed in claim 1 wherein the paddle is of a magnetic material and comprises a liquid moving surface and means for supporting the paddle in or over the chamber and said paddle is caused to undergo a reciprocating motion by the action of an electromagnetic means.

3. A method as claimed in claim 2 wherein the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface which arms sit in a pair of slots in sides extending from a base which defines the chamber.

4. A method as claimed in either claim 2 or 3 which further comprises detecting an analyte in said sample by passing a light beam from a light emitter through said chamber and an opening (106) formed in the liquid moving surface of said paddle to a light detector.

5. A method as claimed in claim 4 wherein the sample is glycated haemoglobin and is detected by a spectrophotometric means at between 405 nm and 460 nm.

6. A paddle (100) comprising a liquid moving surface and means for supporting said paddle in or over a chamber such that the paddle can undergo a reciprocating motion in the chamber.

7. A paddle as claimed in claim 6 wherein the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface.

8. A paddle as claimed in either claim 6 or 7 wherein the paddle is T shaped.

9. A paddle as claimed in any of claim 6,7 or 8 wherein the liquid moving surface has an opening (106) formed therein through which a light beam can pass.

10. A paddle as claimed in any of claims 6 to 9 wherein the paddle comprises a magnetic material.

11. A paddle as claimed in any of claims 6 to 9 wherein the paddle comprises a piezoelectric material.

12. A sample container comprising a chamber (3, 5) adapted to receive a paddle (100), said paddle being mounted in or over said chamber such that the paddle can undergo a reciprocating motion in the chamber.

13. A sample container as claimed in claim 12 comprising a base with sides extending therefrom to define the chamber, said sides comprising means which support the paddle.

14. A sample container as claimed in claim 13 wherein said means which support the paddle is a pair of slots in said sides.

15. A sample container as claimed in any of claims 12-14 in which said chamber is an optical chamber.

16. A sample container as claimed in any of claims 12-15 which is a carousel or cassette.

17. A carousel as claimed in claim 16, for use in an assay in which a sample is separated into a first component fraction and a second component fraction, which fractions are presented to an instrument, comprising a first inlet which is or leads to a first component fraction collection chamber, a second inlet which is or leads to a second component fraction collection chamber, and an inlet port accommodating a filter means or a binder retaining means, said inlet port being movable relative to each of said first and second inlets such that the inlet port can be brought into liquid communication with each first and second inlet in turn as required.

18. A sample container as claimed in claim 16 which is a carousel comprising a base portion having a plurality of chambers including first and second inlets, a top portion which together with the base portion forms the carousel, and a funnel portion including an inlet port, said carousel being rotatably mounted about said funnel portion.

19. An instrument adapted to receive a sample container comprising a chamber adapted to receive a paddle, said instrument comprising means for causing said paddle to undergo a reciprocating motion in the chamber.

20. An apparatus as claimed in claim 19 in which said means for causing said paddle to undergo a reciprocating motion is an electromagnetic means.

21. An apparatus as claimed in claim 20 wherein said electromagnetic means is a solenoid.

22. A device comprising an instrument capable of detecting an analyte in a sample which is presented thereto in a sample container comprising a chamber adapted to receive a paddle said paddle being mounted in or over said chamber such that said paddle can undergo a reciprocating motion when initiated by said instrument.

23. A device, comprising an instrument for reading one or more samples, and an apparatus for presenting the one or more samples to the instrument, wherein the positioning of the one or more samples into a reading position is achieved using two phased recognition.

24. A device as claimed in claim 23 in which a first switch informs the instrument that the apparatus is within range and a second switches confirms precise alignment.

25. A device as claimed in claim 23 or 24 wherein a first micro switch on the instrument is activated by an "element" on the apparatus and this constitutes the first phase of detection and a second switch on the instrument serves as the "fine tune" and is activated when the instrument reaches a precise location on the instrument.

26. A device as claimed in claim 25 wherein the "element" on the apparatus is a projecting member which depresses a board mounted micro-switch via a rocker arm assembly.

27. A device as claimed in claim 26 wherein the two members of the switch are a notch in the outermost wall of the apparatus, and a resilient member or arm on the instrument.

28. A device as claimed in claim 27 wherein the apparatus is a carousel or cassette type apparatus.

29. A device as claimed in claim 28 comprising four switches located 90° apart.

30. A method for determining the percentage glycation of blood comprising separating a blood sample into a first component fraction containing one or more non glycated proteins, and a second component containing the one or more glycated proteins, and detecting/quantifying glycated haemoglobin by spectrophotometric means at between 405 nm and 460 nm.

31. A method as claimed in claim 30 wherein the detection/quantification of glycated haemoglobin is measured at about 440nm.

32. An apparatus incorporating one or a plurality of means for breaking the surface tension of a drop to ensure it leaves a first component part and enters a second component part of an apparatus.

33. An apparatus as claimed in claim 32 in which the means comprise a web or like member situated between the first and second component parts.

34. An apparatus as claimed in claim 32 or 33 wherein the apparatus is of a type in which an inlet port is movable relative to each of first and second inlets which are or lead to first and second collection chambers, said inlet port being a funnel and accommodating a filter means or binder retaining means, said web being situated across an outlet of said funnel.

35. A device comprising an instrument for reading one or more samples and an apparatus for presenting the one or more sample to the instrument, wherein the apparatus is held firmly in position in the instrument by means of spring clips.

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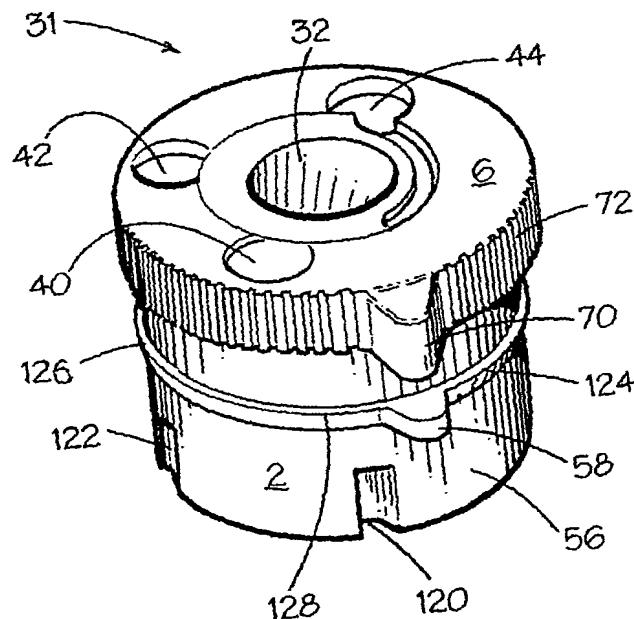
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[Continued on next page]

(54) Title: **MIXING APPARATUS AND METHOD OF MIXING**



WO 00/76642 A2

(57) Abstract: Apparatus, instrument, device and a method of mixing for conducting an assay. Apparatus comprising a first and second inlet and an inlet port accommodating a filter and/or binder retaining means, the inlet port moveable relative to first and second inlets such that the port can be brought into liquid communication with each inlet, and a sample chamber comprising a paddle which undergoes a reciprocating motion.

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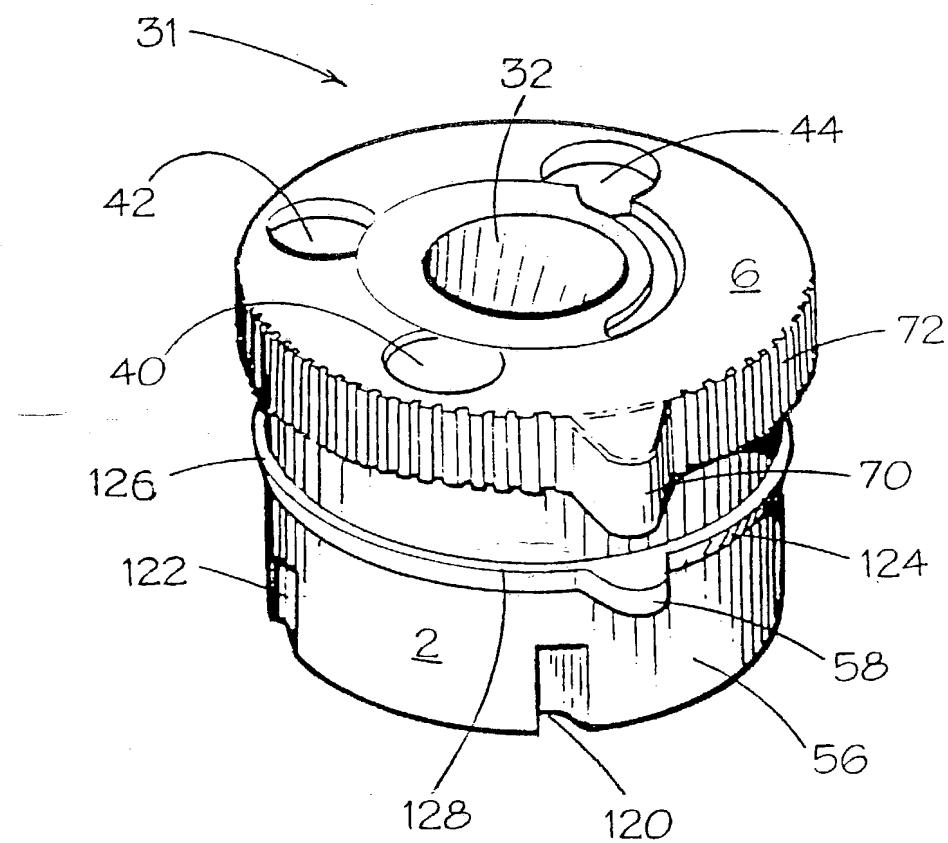


FIG. 1.

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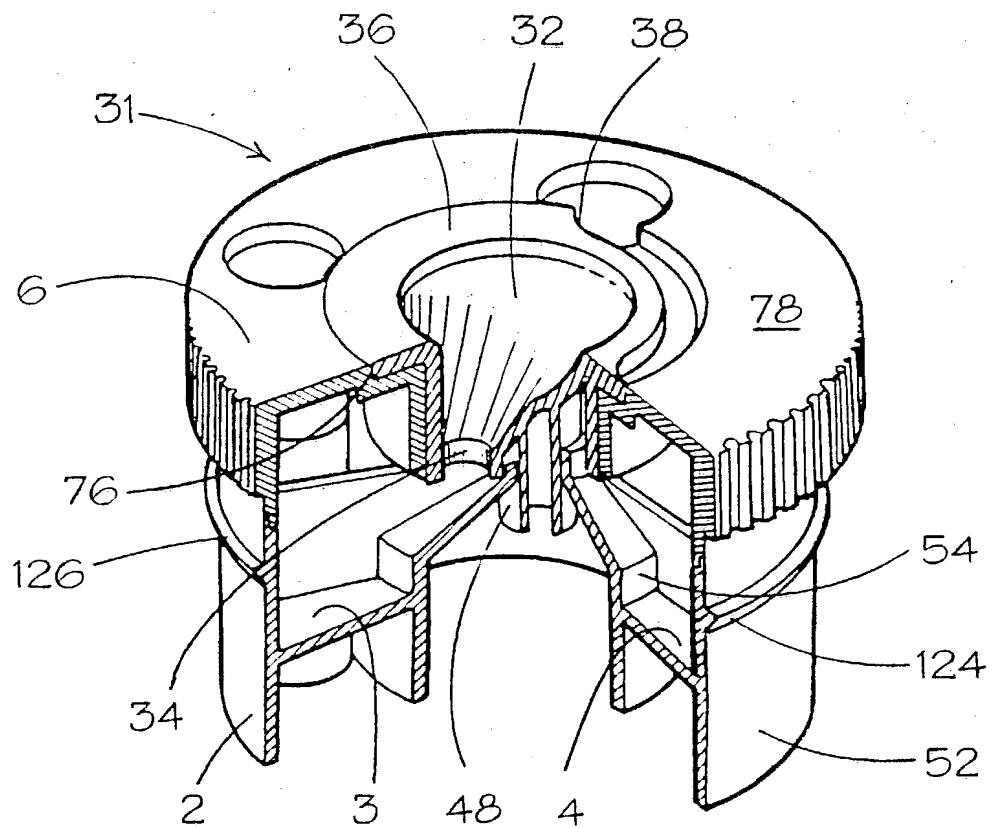


FIG. 2.

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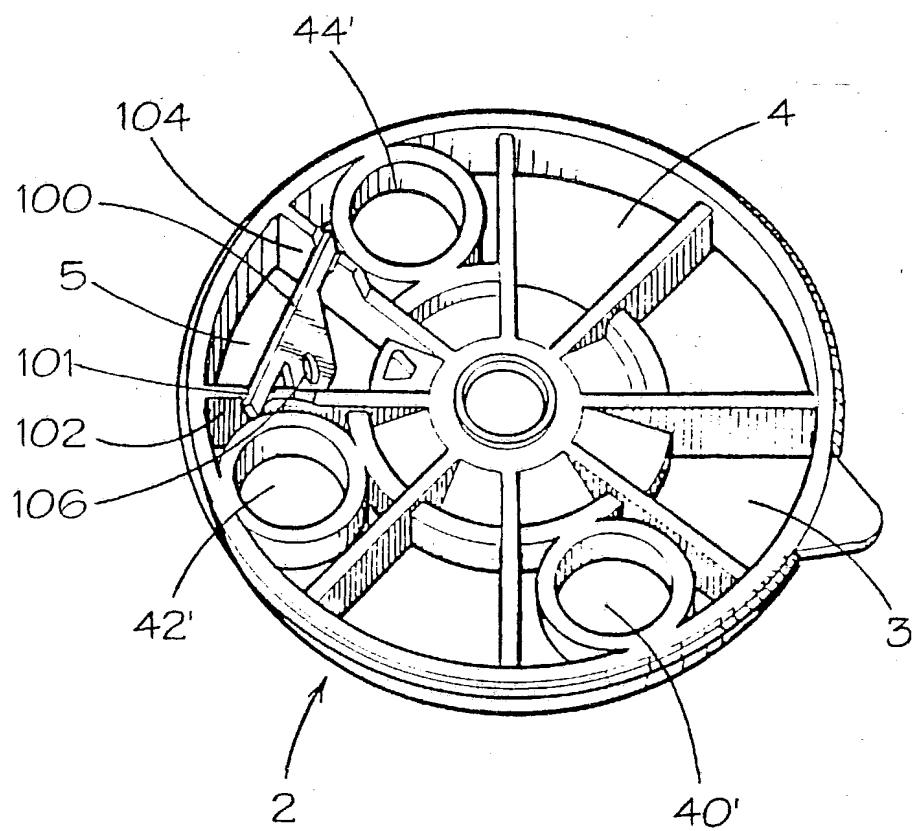


FIG. 3.

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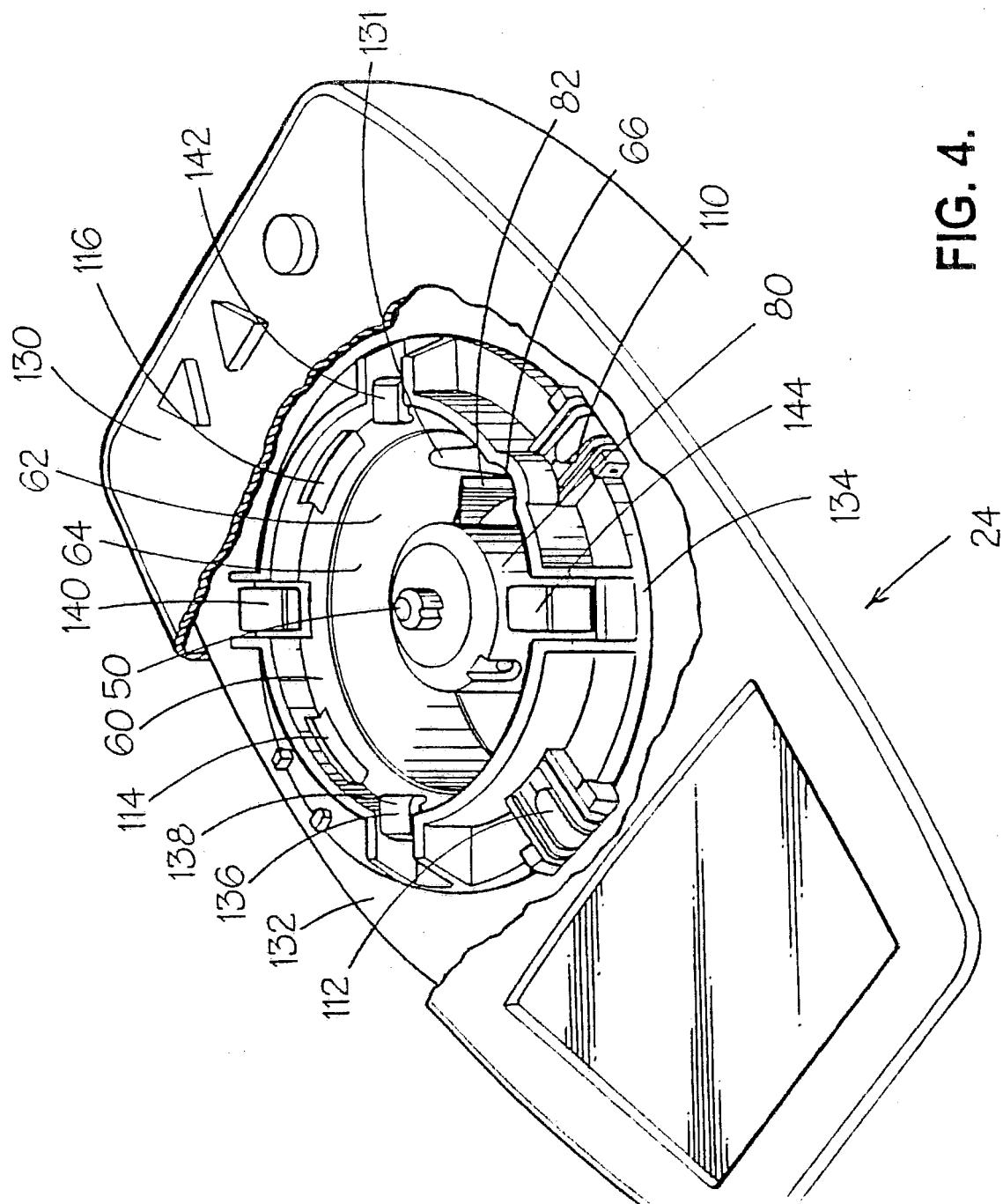


FIG. 4.

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|---|--|-----------------------------|-------------------------------|
| DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63) | | Attorney Docket No. | WPT0006 |
| <input type="checkbox"/> Declaration Submitted with Initial Filing OR <input checked="" type="checkbox"/> Declaration to be Submitted after Initial Filing surcharge 37 CFR 1.16(c) required | | First Named Inventor | David ANDREWES, et al. |
| COMPLETE IF KNOWN | | | |
| Application Number: | | 10/009,277 | |
| Filing Date: | | December 7, 2001 | |
| Group Art Unit: | | | |
| Examiner Name: | | | |

As a below named Inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**MIXING APPARATUS AND METHOD OF MIXING DURING
CONDUCTING AN ASSAY**

the specification of which

is attached hereto

OR

was filed on
(MM/DD/YYYY)

12/07/2001

as U.S. Application No. or
PCT International Application No.

and was amended on
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(if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I hereby claim foreign priority benefits under 35 U.S.C. § 119(a)-(d) or 365(b) of any foreign application(s) for patent or Inventor's certificate, or § 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or Inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed.

| Prior Foreign Appl. No.(s) | Country | Foreign Filing Date (MM/DD/YYYY) | Priority Not Claimed | Certified Copy Attached? Yes | No |
|-----------------------------|------------|-------------------------------------|--|--|--|
| PCT/GB00/02259 9913560.0 | WIPO GB | 06/09/2000 06/10/1999 | <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> | <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> | <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> |
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Additional foreign application nos. are listed on a supplemental priority data sheet PTO/SB/02B attached hereto:

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Application Number(s) Filing Date (MM/DD/YYYY)

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U.S. Parent Application or PCT Parent No.

**Parent Filing Date
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**Parent Patent No.
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[Page 2 of 2]

DECLARATION

ADDITIONAL INVENTOR(S)
Supplemental Sheet
 Page 1 of 4

| | | | | | | | | |
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| DECLARATION | | | | ADDITIONAL INVENTOR(S) Supplemental Sheet Page <u>2</u> of <u>4</u> | | | | |
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| <u>Mark</u> | | | | | | | CRESSWELL | |
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| U.S. Parent Application or PCT Parent No. | Parent Filing Date (MM/DD/YY) | Parent Patent No. (if applicable) |
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| Given Name (first and middle [if any]) | Family Name or Surname |
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| | |
|-------|----------|
| David | ANDREWES |
|-------|----------|

| | | | | | | | | |
|----------------------|-----------------|-------|-------------|---------|---------|-------------|------|--|
| Inventor's Signature | | | | | | | Date | |
| Residence City | Farnham | State | Surrey (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | 5 Ridgeway Road | | | | | | | |
| Post Office Address | | | | | | | | |
| City | Farnham | State | Surrey (GB) | ZIP | GU9 8NN | Country | UK | |

Additional inventors are named on 3 supplemental additional inventor(s) sheet(s) PTO/SB/02A attached

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| DECLARATION | ADDITIONAL INVENTOR(S) Supplemental Sheet Page <u>1</u> of <u>4</u> |
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|---|-----------------|---|-------------|---------|----------|-------------|------|--|
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | | |
| John Worthington | | ATTRIDGE | | | | | | |
| Inventor's Signature | | | | | | | Date | |
| Residence: City | Ripley | State | Surrey (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | Oaksbridge | | | | | | | |
| Post Office Address | Send Marsh Road | | | | | | | |
| City | Ripley | State | Surrey (GB) | ZIP | CH23 6JR | Country | UK | |
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | | |
| John Philip | | VESSEY | | | | | | |
| Inventor's Signature | | | | | | | Date | |
| Residence: City | East Horsley | State | Surrey (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | Canna | | | | | | | |
| Post Office Address | Forest Road | | | | | | | |
| City | East Horsley | State | Surrey (GB) | ZIP | KT24 5BT | Country | UK | |
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|--|---|---|--------------|---|----------|-------------|----|--|
| DECLARATION | | | | ADDITIONAL INVENTOR(S) Supplemental Sheet Page <u>2</u> of <u>4</u> | | | | |
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | | |
| Felix | | FERNANDO | | | | | | |
| Inventor's Signature | | | | | | Date | | |
| Residence: City | Wokingham | State | Berks (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | 24 Tudor Close | | | | | | | |
| Post Office Address | | | | | | | | |
| City | Wokingham | State | Berks (GB) | ZIP | RG40 2LU | Country | UK | |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | | |
| Anthony | STEVENSON | | | | | | | |
| Inventor's Signature | | | | | | Date | | |
| Residence: City | Chester | State | Chester (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | 4 Beaumont Close | | | | | | | |
| Post Office Address | | | | | | | | |
| City | Chester | State | Chester (GB) | ZIP | CH4 8PT | Country | UK | |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | | |
| Mark | CRESSWELL | | | | | | | |
| Inventor's Signature | | | | | | Date | | |
| Residence: City | Broughton | State | Chester (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | 11 Main Road | | | | | | | |
| Post Office Address | | | | | | | | |
| City | Broughton | State | Chester (GB) | ZIP | CH4 0NW | Country | UK | |

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|--|---|---|-----------------|---|---------|-------------|----|
| DECLARATION | | | | ADDITIONAL INVENTOR(S) Supplemental Sheet Page <u>3</u> of <u>4</u> | | | |
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | |
| John | | CURTIS | | | | | |
| Inventor's Signature | | | | | | Date | |
| Residence: City | Balderton | State | Chester (GB) | Country | UK | Citizenship | UK |
| Post Office Address | Balderton House | | | | | | |
| Post Office Address | | | | | | | |
| City | Balderton | State | Chester (BG) | ZIP | CH4 9FL | Country | UK |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | |
| David Alan | PERCIVAL | | | | | | |
| Inventor's Signature | | | | | | Date | |
| Residence: City | Hawarden | State | Flintshire (GB) | Country | UK | Citizenship | UK |
| Post Office Address | 4 Overlea Drive | | | | | | |
| Post Office Address | | | | | | | |
| City | Hawarden | State | Flintshire (GB) | ZIP | CH5 3HS | Country | UK |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | |
| John Anthony | O'DELL | | | | | | |
| Inventor's Signature | | | | | | Date | |
| Residence: City | Balderton | State | London (GB) | Country | UK | Citizenship | UK |
| Post Office Address | 24 Halford Road | | | | | | |
| City | Fulham | State | London (GB) | ZIP | SW6 1JT | Country | UK |

DECLARATION – Utility or Design Patent Application

I hereby claim the benefit under 35 U.S.C. 120 of any U.S. application(s) or 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of 35 U.S.C. 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

| U.S. Parent Application or PCT Parent No. | Parent Filing Date (MM/DD/YY) | Parent Patent No. (if applicable) |
|---|----------------------------------|--------------------------------------|
| | | |

Additional U.S. or PCT international application nos. listed on PTO/SB/02B attached hereto.

As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent Trademark Office connected therewith:

Customer Number

OR

Registered practitioner(s) name/registration number listed below

| Name | Registration Number | Name | Registration Number |
|------|------------------------|------|------------------------|
| | | | |

Additional registered practitioner(s) named on supplemental sheet PTO/SB/02C attached hereto.

Direct all correspondence to: Customer Number **25235** OR Correspondence address below
or Bar Code Label PATENT TRADEMARK OFFICE

| | | | | | | | |
|---------|--|-----------|--|-------|--|-----|--|
| Name | | | | | | | |
| Address | | | | | | | |
| Address | | | | | | | |
| City | | | | State | | ZIP | |
| Country | | Telephone | | | | Fax | |

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and such willful false statements may jeopardize the validity of the application or any patent issued thereon.

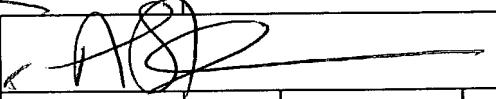
Name of Sole or First Inventor: A petition has been filed for this unsigned inventor.

| | | | | | | | | |
|--|------------------------|-------|-------------|------------------------|---------|-------------|------|--|
| Given Name (first and middle [if any]) | | | | Family Name or Surname | | | | |
| David | | | | ANDREWES | | | | |
| Inventor's Signature | | | | | | | Date | |
| Residence City | Farnham | State | Surrey (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | 5 Ridgeway Road | | | | | | | |
| Post Office Address | | | | | | | | |
| City | Farnham | State | Surrey (GB) | ZIP | GU9 8NN | Country | UK | |

Additional inventors are named on 3 supplemental additional inventor(s) sheet(s) PTO/SB/02A attached

| | |
|--------------------|---|
| DECLARATION | ADDITIONAL INVENTOR(S) Supplemental Sheet Page <u>1</u> of <u>4</u> |
|--------------------|---|

| | | | | | | | |
|--|-----------------|---|-------------|---------|----------|-------------|----|
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | |
| John Worthington | | ATTRIDGE | | | | | |
| Inventor's Signature | | | | | | Date | |
| Residence: City | Ripley | State | Surrey (GB) | Country | UK | Citizenship | UK |
| Post Office Address | Oaksbridge | | | | | | |
| Post Office Address | Send Marsh Road | | | | | | |
| City | Ripley | State | Surrey (GB) | ZIP | CH23 6JR | Country | UK |
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| John Philip | | VESSEY | | | | | |
| Inventor's Signature | | | | | | Date | |
| Residence: City | East Horsley | State | Surrey (GB) | Country | UK | Citizenship | UK |
| Post Office Address | Canna | | | | | | |
| Post Office Address | Forest Road | | | | | | |
| City | East Horsley | State | Surrey (GB) | ZIP | KT24 5BT | Country | UK |
| | | | | | | | |

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|--|---|---|--------------|---|----------|-------------|----|
| DECLARATION | | | | ADDITIONAL INVENTOR(S) Supplemental Sheet Page <u>2</u> of <u>4</u> | | | |
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | |
| Felix | | FERNANDO | | | | | |
| Inventor's Signature | | | | | Date | | |
| Residence: City | Wokingham | State | Berks (GB) | Country | UK | Citizenship | UK |
| Post Office Address | 24 Tudor Close | | | | | | |
| Post Office Address | | | | | | | |
| City | Wokingham | State | Berks (GB) | ZIP | RG40 2LU | Country | UK |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | |
| Anthony | STEVENSON | | | | | | |
| Inventor's Signature |  | | | | Date | 03/04/02 | |
| Residence: City | Chester | State | Chester (GB) | Country | UK | Citizenship | UK |
| Post Office Address | 4 Beaumont Close 6 BX | | | | | | |
| Post Office Address | | | | | | | |
| City | Chester | State | Chester (GB) | ZIP | CH4 8PT | Country | UK |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | |
| Mark | CRESSWELL | | | | | | |
| Inventor's Signature | | | | | Date | | |
| Residence: City | Broughton | State | Chester (GB) | Country | UK | Citizenship | UK |
| Post Office Address | 11 Main Road | | | | | | |
| Post Office Address | | | | | | | |
| City | Broughton | State | Chester (GB) | ZIP | CH4 0NW | Country | UK |

| DECLARATION | | | | ADDITIONAL INVENTOR(S) Supplemental Sheet Page <u>3</u> of <u>4</u> | | | |
|--|---|---|-----------------|---|---------|-------------|----|
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | |
| John | | CURTIS | | | | | |
| Inventor's Signature | | | | | | Date | |
| Residence: City | Balderton | State | Chester (GB) | Country | UK | Citizenship | UK |
| Post Office Address | Balderton House | | | | | | |
| Post Office Address | | | | | | | |
| City | Balderton | State | Chester (BG) | ZIP | CH4 9FL | Country | UK |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | |
| David Alan | PERCIVAL | | | | | | |
| Inventor's Signature | | | | | | Date | |
| Residence: City | Hawarden | State | Flintshire (GB) | Country | UK | Citizenship | UK |
| Post Office Address | 4 Overlea Drive | | | | | | |
| Post Office Address | | | | | | | |
| City | Hawarden | State | Flintshire (GB) | ZIP | CH5 3HS | Country | UK |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | |
| John Anthony | O'DELL | | | | | | |
| Inventor's Signature | | | | | | Date | |
| Residence: City | Balderton | State | London (GB) | Country | UK | Citizenship | UK |
| Post Office Address | 24 Halford Road | | | | | | |
| City | Fulham | State | London (GB) | ZIP | SW6 1JT | Country | UK |

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|--------------------|---|
| DECLARATION | ADDITIONAL INVENTOR(S) Supplemental Sheet Page <u>4</u> of <u>4</u> |
|--------------------|---|

| | | | | | | | |
|--|---|-------|--------------|---------|---------|-------------|----|
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | |
| Adrian Richard | GRAY | | | | | | |
| Inventor's Signature | | | | | | Date | |
| Residence: City | Vaughans Lane | State | Chester (GB) | Country | UK | Citizenship | UK |
| Post Office Address | West End House | | | | | | |
| Post Office Address | | | | | | | |
| City | Vaughans Lane | State | Chester (BG) | ZIP | CH3 5XF | Country | UK |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | |
| | | | | | | | |
| Inventor's Signature | | | | | | Date | |
| Residence: City | | State | | Country | | Citizenship | |
| Post Office Address | | | | | | | |
| Post Office Address | | | | | | | |
| City | | State | | ZIP | | Country | |

**DECLARATION FOR
UTILITY OR DESIGN
PATENT APPLICATION
(37 CFR 1.63)**

Declaration Submitted with Initial Filing Declaration to be Submitted after Initial Filing-- surcharge 37 CFR 1.16(e) required

| | |
|--------------------------|------------------------|
| Attorney Docket No. | WPT0006 |
| First Named Inventor | David ANDREWES, et al. |
| COMPLETE IF KNOWN | |
| Application Number | 10/009,277 |
| Filing Date | December 7, 2001 |
| Group Art Unit | |
| Examiner Name | |

As a below named Inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**MIXING APPARATUS AND METHOD OF MIXING DURING
CONDUCTING AN ASSAY**

the specification of which

is attached hereto

OR

was filed on
(MM/DD/YYYY)

12/07/2001

as U.S. Application No. or
PCT International Application No.

and was amended on
(MM/DD/YYYY)

(if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I hereby claim foreign priority benefits under 35 U.S.C § 119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed.

| Prior Foreign Appl. No.(s) | Country | Foreign Filing Date (MM/DD/YYYY) | Priority Not Claimed | Certified Copy Attached? Yes | Certified Copy Attached? No |
|----------------------------|---------|-------------------------------------|--------------------------|---------------------------------|-------------------------------------|
| PCT/GB00/02259 | WIPO | 06/09/2000 | <input type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| 9913560.0 | GB | 06/10/1999 | <input type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| | | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| | | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

Additional foreign application nos. are listed on a supplemental priority data sheet PTO/SB/02B attached hereto:

I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States provisional application(s) listed below.

Application Number(s) Filing Date (MM/DD/YYYY)

DECLARATION – Utility or Design Patent Application

I hereby claim the benefit under 35 U.S.C. 120 of any U.S. application(s) or 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of 35 U.S.C. 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

| U.S. Parent Application or PCT Parent No. | Parent Filing Date (MM/DD/YY) | Parent Patent No. (if applicable) |
|---|----------------------------------|--------------------------------------|
| | | |

Additional U.S. or PCT international application nos. listed on PTO/SB/02B attached hereto.

As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent Trademark Office connected therewith:

Customer Number

OR

Registered practitioner(s) name/registration number listed below

| Name | Registration Number | Name | Registration Number |
|------|---------------------|------|---------------------|
| | | | |

Additional registered practitioner(s) named on supplemental sheet PTO/SB/02C attached hereto.

Direct all correspondence to: Customer Number **25235** OR Correspondence address below
or Bar Code Label PATENT TRADEMARK OFFICE

| | | | | | | | |
|---------|--|-----------|--|-------|--|-----|--|
| Name | | | | | | | |
| Address | | | | | | | |
| Address | | | | | | | |
| City | | | | State | | ZIP | |
| Country | | Telephone | | | | Fax | |

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor: A petition has been filed for this unsigned inventor.

| | |
|--|------------------------|
| Given Name (first and middle [if any]) | Family Name or Surname |
|--|------------------------|

| | |
|-------|----------|
| David | ANDREWES |
|-------|----------|

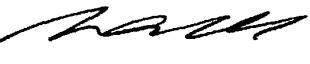
| | | | | | | | | |
|----------------------|-----------------|-------|-------------|---------|---------|-------------|------|--|
| Inventor's Signature | | | | | | | Date | |
| Residence City | Farnham | State | Surrey (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | 5 Ridgeway Road | | | | | | | |
| Post Office Address | | | | | | | | |
| City | Farnham | State | Surrey (GB) | ZIP | GU9 8NN | Country | UK | |

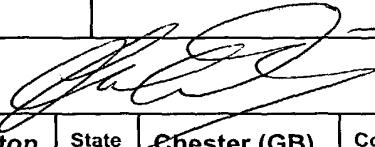
Additional inventors are named on 3 supplemental additional inventor(s) sheet(s) PTO/SB/02A attached

DECLARATION

ADDITIONAL INVENTOR(S)
Supplemental Sheet
Page 1 of 4

| | | | | | | | | |
|--|-----------------|-------|-------------|---|----------|-------------|------|--|
| Name of Additional Joint Inventor, if any: | | | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | |
| Given Name (first and middle [if any]) | | | | Family Name or Surname | | | | |
| John Worthington | | | | ATTRIDGE | | | | |
| Inventor's Signature | | | | | | | Date | |
| Residence: City | Ripley | State | Surrey (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | Oaksbridge | | | | | | | |
| Post Office Address | Send Marsh Road | | | | | | | |
| City | Ripley | State | Surrey (GB) | ZIP | CH23 6JR | Country | UK | |
| Name of Additional Joint Inventor, if any: | | | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | |
| Given Name (first and middle [if any]) | | | | Family Name or Surname | | | | |
| John Philip | | | | VESSEY | | | | |
| Inventor's Signature | | | | | | | Date | |
| Residence: City | East Horsley | State | Surrey (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | Canna | | | | | | | |
| Post Office Address | Forest Road | | | | | | | |
| City | East Horsley | State | Surrey (GB) | ZIP | KT24 5BT | Country | UK | |
| | | | | | | | | |

| DECLARATION | | | | ADDITIONAL INVENTOR(S) Supplemental Sheet Page <u>2</u> of <u>4</u> | | | |
|--|--|---|--------------|---|----------|-------------|---------|
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | |
| Felix | | FERNANDO | | | | | |
| Inventor's Signature | | | | | | Date | |
| Residence: City | Wokingham | State | Berks (GB) | Country | UK | Citizenship | UK |
| Post Office Address | 24 Tudor Close | | | | | | |
| Post Office Address | | | | | | | |
| City | Wokingham | State | Berks (GB) | ZIP | RG40 2LU | Country | UK |
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| Anthony | STEVENSON | | | | | | |
| Inventor's Signature | | | | | | Date | |
| Residence: City | Chester | State | Chester (GB) | Country | UK | Citizenship | UK |
| Post Office Address | 4 Beaumont Close | | | | | | |
| Post Office Address | | | | | | | |
| City | Chester | State | Chester (GB) | ZIP | CH4 8PT | Country | UK |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | |
| Mark | CRESSWELL | | | | | | |
| Inventor's Signature |  | | | | | Date | 27/3/02 |
| Residence: City | Broughton | State | Chester (GB) | Country | UK | Citizenship | UK |
| Post Office Address | 11 Main Road  | | | | | | |
| Post Office Address | | | | | | | |
| City | Broughton | State | Chester (GB) | ZIP | CH4 0NW | Country | UK |

| DECLARATION | | | | ADDITIONAL INVENTOR(S) Supplemental Sheet Page <u>3</u> of <u>4</u> | | | |
|--|---|---|-----------------|---|---------|-------------|----------------|
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | |
| <u>John</u> | | <u>CURTIS</u> | | | | | |
| Inventor's Signature |  | | | | | Date | <u>28/3/02</u> |
| Residence: City | Balderton | State | Chester (GB) | Country | UK | Citizenship | UK |
| Post Office Address | <u>Balderton House</u> GBX | | | | | | |
| Post Office Address | | | | | | | |
| City | Balderton | State | Chester (BG) | ZIP | CH4 9FL | Country | UK |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | |
| <u>David Alan</u> | <u>PERCIVAL</u> | | | | | | |
| Inventor's Signature |  | | | | | Date | <u>28/3/02</u> |
| Residence: City | Hawarden | State | Flintshire (GB) | Country | UK | Citizenship | UK |
| Post Office Address | <u>4 Overlea Drive</u> GBX | | | | | | |
| Post Office Address | | | | | | | |
| City | Hawarden | State | Flintshire (GB) | ZIP | CH5 3HS | Country | UK |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | |
| <u>John Anthony</u> | <u>O'DELL</u> | | | | | | |
| Inventor's Signature | | | | | | Date | |
| Residence: City | Balderton | State | London (GB) | Country | UK | Citizenship | UK |
| Post Office Address | <u>24 Halford Road</u> | | | | | | |
| City | Fulham | State | London (GB) | ZIP | SW6 1JT | Country | UK |

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| DECLARATION | | ADDITIONAL INVENTOR(S) Supplemental Sheet Page <u>4</u> of <u>4</u> |
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| | | | | | | | | |
|--|---|---|--------------|---------|---------|-------------|------|--|
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | | |
| Adrian Richard | | GRAY | | | | | | |
| Inventor's Signature | | | | | | | Date | |
| Residence: City | Vaughans Lane | State | Chester (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | West End House | | | | | | | |
| Post Office Address | | | | | | | | |
| City | Vaughans Lane | State | Chester (BG) | ZIP | CH3 5XF | Country | UK | |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | | |
| | | | | | | | | |
| Inventor's Signature | | | | | | | Date | |
| Residence: City | | State | | Country | | Citizenship | | |
| Post Office Address | | | | | | | | |
| Post Office Address | | | | | | | | |
| City | | State | | ZIP | | Country | | |

**DECLARATION FOR
UTILITY OR DESIGN
PATENT APPLICATION
(37 CFR 1.63)**

Declaration Submitted with Initial Filing OR Declaration to be Submitted after Initial Filing-- surcharge 37 CFR 1.16(e) required

| | |
|--------------------------|------------------------|
| Attorney Docket No. | WPT0006 |
| First Named Inventor | David ANDREWES, et al. |
| COMPLETE IF KNOWN | |
| Application Number | 10/009,277 |
| Filing Date | December 7, 2001 |
| Group Art Unit | |
| Examiner Name | |

As a below named Inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**MIXING APPARATUS AND METHOD OF MIXING DURING
CONDUCTING AN ASSAY**

the specification of which

is attached hereto

OR

was filed on
(MM/DD/YYYY)

12/07/2001

as U.S. Application No. or
PCT International Application No.

and was amended on
(MM/DD/YYYY)

(if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I hereby claim foreign priority benefits under 35 U.S.C § 119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed.

| Prior Foreign Appl. No.(s) | Country | Foreign Filing Date (MM/DD/YYYY) | Priority Not Claimed | Certified Copy Attached? Yes | No |
|----------------------------|---------|-------------------------------------|--------------------------|---------------------------------|-------------------------------------|
| PCT/GB00/02259 | WIPO | 06/09/2000 | <input type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| 9913560.0 | GB | 06/10/1999 | <input type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| | | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| | | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

Additional foreign application nos. are listed on a supplemental priority data sheet PTO/SB/02B attached hereto:

I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States provisional application(s) listed below.

Application Number(s) Filing Date (MM/DD/YYYY)

| | | | | | | | |
|---|---|---|---------------------|----------------|----------------|--------------------|-----------|
| DECLARATION | | ADDITIONAL INVENTOR(S) Supplemental Sheet Page <u>4</u> of <u>4</u> | | | | | |
| Name of Additional Joint Inventor, if any: Given Name (first and middle [if any]) Adrian Richard | | <input type="checkbox"/> A petition has been filed for this unsigned inventor Family Name or Surname GRAY | | | | | |
| Inventor's Signature | | | | | Date | | |
| Residence: City | Vaughans Lane | State | Chester (GB) | Country | UK | Citizenship | UK |
| Post Office Address | West End House | | | | | | |
| Post Office Address | | | | | | | |
| City | Vaughans Lane | State | Chester (BG) | ZIP | CH3 5XF | Country | UK |
| Name of Additional Joint Inventor, If any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | |
| Inventor's Signature | | | | | Date | | |
| Residence: City | | State | | Country | | Citizenship | |
| Post Office Address | | | | | | | |
| Post Office Address | | | | | | | |
| City | | State | | ZIP | | Country | |

| | | | | | | | | |
|--|---|---|-----------------|--|---------|-------------|------------------|--|
| DECLARATION | | | | ADDITIONAL INVENTOR(S) Supplemental Sheet Page <u>3</u> of <u>4</u> | | | | |
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | | |
| John | | CURTIS | | | | | | |
| Inventor's Signature | | | | | | | Date | |
| Residence: City | Balderton | State | Chester (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | Balderton House | | | | | | | |
| Post Office Address | | | | | | | | |
| City | Balderton | State | Choster (BG) | ZIP | CH4 9FL | Country | UK | |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | | |
| David Alan | PERCIVAL | | | | | | | |
| Inventor's Signature | | | | | | | Date | |
| Residence: City | Hawarden | State | Flintshire (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | 4 Overlea Drive | | | | | | | |
| Post Office Address | | | | | | | | |
| City | Hawarden | State | Flintshire (GB) | ZIP | CH5 3HS | Country | UK | |
| Name of Additional Joint Inventor, if any: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | | | | |
| John Anthony | O'DELL | | | | | | | |
| Inventor's Signature | Anthony O'Dell | | | | | | 14-6-'02 Date | |
| Residence: City | Balderton | State | London (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | 24 Halford Road GBX | | | | | | | |
| City | Fulham | State | London (GB) | ZIP | SW6 1JT | Country | UK | |

| | | | |
|---|--|-----------------------------|-------------------------------|
| DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63) | | Attorney Docket No. | WPT0006 |
| <input type="checkbox"/> Declaration Submitted with Initial Filing OR <input checked="" type="checkbox"/> Declaration to be Submitted after Initial Filing-- surcharge 37 CFR 1.16(e) required | | First Named Inventor | David ANDREWES, et al. |
| COMPLETE IF KNOWN | | | |
| Application Number | | 10/009,277 | |
| Filing Date | | December 7, 2001 | |
| Group Art Unit | | | |
| Examiner Name | | | |

As a below named Inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**MIXING APPARATUS AND METHOD OF MIXING DURING
CONDUCTING AN ASSAY**

the specification of which

is attached hereto

OR

was filed on
(MM/DD/YYYY)

12/07/2001

as U.S. Application No. or
PCT International Application No. _____

and was amended on
(MM/DD/YYYY)

(if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I hereby claim foreign priority benefits under 35 U.S.C § 119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed.

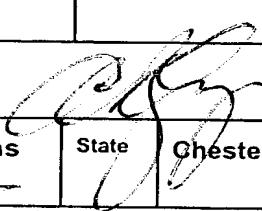
| Prior Foreign Appl. No.(s) | Country | Foreign Filing Date (MM/DD/YYYY) | Priority Not Claimed | Certified Copy Attached? Yes | Certified Copy Attached? No |
|----------------------------|---------|-------------------------------------|--------------------------|---------------------------------|-------------------------------------|
| PCT/GB00/02259 | WIPO | 06/09/2000 | <input type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| 9913560.0 | GB | 06/10/1999 | <input type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| | | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| | | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

Additional foreign application nos. are listed on a supplemental priority data sheet PTO/SB/02B attached hereto:

I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States provisional application(s) listed below.

Application Number(s) Filing Date (MM/DD/YYYY)

DECLARATION**ADDITIONAL INVENTOR(S)**
Supplemental Sheet
Page 4 of 4

| | | | | | | | | |
|---|---|---|--------------|---------|---------|-------------|------|------------|
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | | |
| <u>Adrian Richard</u> | | <u>GRAY</u> | | | | | | |
| Inventor's Signature |  | | | | | | Date | 24 July 02 |
| Residence: City | Vaughans Lane | State | Chester (GB) | Country | UK | Citizenship | UK | |
| Post Office Address | West End House GBX | | | | | | | |
| Post Office Address | | | | | | | | |
| City | Vaughans Lane | State | Chester (BG) | ZIP | CH3 5XF | Country | UK | |
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | | |
| | | | | | | | | |
| Inventor's Signature | | | | | | | Date | |
| Residence: City | | State | | Country | | Citizenship | | |
| Post Office Address | | | | | | | | |
| Post Office Address | | | | | | | | |
| City | | State | | ZIP | | Country | | |